CLAIMS

1. A method of identifying therapeutic agents, which induce cell maturation or cell death, the method comprising:

contacting test cells with a potential therapeutic agent wherein said test cells contain established levels of DM or extrachromosomal DNA and are capable of undergoing micronucleation; and

assaying said test cells for the level of DM or extrachromosomal DNA, whereby reduction or elimination of DM or extrachromosomal DNA from the cells indicates that the agent is a therapeutic agent that promotes micronucleation which results in cell maturation or cell death.

2. The method of claim 1, wherein the test cells lack functional tumor suppressor protein.

3. The method of claim 1, wherein the test cells contain an oncogene.

4. The method of claim 1, wherein assaying is conducted by FISH, flow cytometry, centrifugal fractionization or histone-GFP labeling.

5. A therapeutic agent identified by the method of claim 1.

6. A method for inducing maturation or death of a suitable cell, the method comprising contacting the suitable cell with an agent that induces or enhances elimination of DM or extrachromosomal DNA from the suitable cell by micronucleation.

7. The method of claim 6, wherein the cell lacks functional tumor suppressor protein.

8. The method of claim 6, wherein the suitable cell contains an amplified oncogene.

9. The method of claim 6, wherein the suitable cells are contacted *in vitro*, *ex vivo* or *in vivo*.

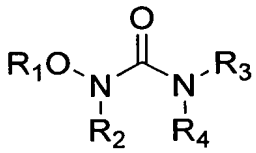
10. A method of treating a subject with a disease relates to the presence in the subject of cells containing DM or extrachromosomal DNA and the capacity to eliminate DM or DNA by extra micronucleation, the method comprising administering to the subject an effective amount of an agent that induces or enhances elimination of DM or extra chromosomal DNA by micronucleation from the cells.

11. The method of claim 10, wherein the cells lack a functional tumor suppressor protein.

12. The method of claim 10, wherein the cells contain an amplified oncogene.

13. The method of claim 10, wherein the agent is hydroxyurea or a derivative thereof.

14. The method of claim 6 or 10, wherein the agent is a compound having the formula:



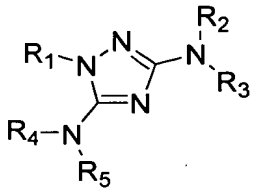
wherein R_1 is H, alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, acyl or $-(CH_2)_n-X$, wherein n is an integer from 1 to 4, X is substituted alkyl, alkenyl or alkynyl, and substituents are selected from the group consisting of halo, $-OH$, $-NR_2$, $-OR$, $-C(O)OR$, $-OC(O)R$, amide and acyl wherein R is H, alkyl or aryl;

R_2 is H, alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, –C(O)R' or $-(CH_2)_n-X$, wherein n is an integer from 1 to 4, X is substituted alkyl, alkenyl or alkynyl, and wherein R' is alkyl or aryl and substituents are as defined above;

R_3 is H, alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, OR'', NR''_2 or $-(CH_2)_n-X$, wherein n is an integer from 1 to 4, X is substituted alkyl, alkenyl or alkynyl, and substituents are selected from the group consisting of –OH, $-NR''_2$, –OR'', –C(O)OR'', –OC(O)R'', amide and acyl wherein R'' is H, alkyl or aryl; and

R_4 is H, alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, or $-(CH_2)_n-X$, wherein n is an integer from 1 to 4, X is substituted alkyl, alkenyl or alkynyl, and substituents are selected from the group consisting of –OH, $-NR'''_2$, –OR''', –C(O)OR''', –OC(O)R''', amide and acyl wherein R''' is H, alkyl or aryl.

15. The method of claim 6 or 10, wherein the agent is a compound having the formula:



wherein R_1 is H, alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, acyl or $-(CH_2)_n-X$, wherein n is an integer from 1 to 4, X is substituted alkyl, alkenyl or alkynyl, and substituents are selected from the group consisting of halo, –OH, $-NR_2$, –OR, –C(O)OR, –OC(O)R, amide and acyl wherein R is H, alkyl or aryl;

R_2 and R_4 are independently H, alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, OR', NR'_2 or $-(CH_2)_n-X$, wherein n is an integer from 1 to 4, X is substituted alkyl, alkenyl or alkynyl, and substituents are selected

from the group consisting of –OH, –NR'$_2$, –OR', –C(O)OR', –OC(O)R', amide and acyl wherein R' is H, alkyl or aryl; and

R_3 and R_5 are independently H, alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl or $-(CH_2)_n-X$, wherein n is an integer from 1 to 4, n is an integer from 1 to 4; X is substituted alkyl, alkenyl or alkynyl, and substituents are selected from the group consisting of –OH, –NR''$_2$, –OR'', –C(O)OR'', –OC(O)R'', amide and acyl wherein R'' is H, alkyl or aryl.

16. A method of detecting DM or extrachromosomal DNA in a cell, the method comprising the steps of:

introducing into the cell a detectably labeled protein, wherein the protein specifically associates with DM and extrachromosomal DNA in the cell; and

detecting the complex of labeled protein and/or DM or extrachromosomal DNA thereby indicating the pressure of DM and extrachromosomal DNA in the cell.

17. The method of claim 16, wherein the protein is histone or an analog thereof.

18. The method of claim 16, wherein the detectable label is a fluorescent label.

19. The method of claim 18, wherein the fluorescent label is Aequorea victoria green fluorescent protein, Aequorea victoria cayenne fluorescent protein or Aequorea victoria yellow fluorescent protein.

20. The method of claim 16 wherein the labeled protein is introduced into the cell by contacting the cell with a vector comprising a DNA encoding detectably labeled histone fusion protein.

21. The method of claim 20 wherein the histone fusion protein is H2B-GFP.

22. The method of claim 20, wherein the vector is a retroviral vector.

23. A method for monitoring the movement of chromosomal DNA material in a cell, comprising:

introducing into the cell a detectably labeled protein, wherein the protein specifically associates with chromosomal DNA in the cell to provide a labeled complex;

detecting labeled complex thereby detecting chromosomal DNA in the cell; and

comparing the location of the labeled complex with uncomplexed chromosome.

24. The method of claim 23, wherein the protein that specifically associates with the chromosomal DNA in the cell is centromere binding protein or lac operator.

25. The method of claim 23, wherein the movement of the chromosome is selected from the group consisting of chromosome condensation, chromosome decondensation, nucleolar formation, heterochromatin movement, chromosome fragmentation, chromosome bridge formation, micronucleation, gene amplification, formation of aneuploidy, chromosome loss and chromosome translocation.

26. A method of detecting a pathological cell phenotype, the method comprising:

introducing into the cell a detectably labeled protein, wherein the protein specifically associates with DM and extrachromosomal DNA to provide a labeled complex;

detecting the labeled complex, thereby detecting DM and extrachromosomal DNA associated with the pathological phenotype; and

comparing the pathological phenotype with the phenotype of a reference cell.

27. The method of claim 26, wherein the pathological phenotype is cancer or a neoplastic disease.